

WHAT IS CLAIMED:

1. A method for characterizing regulatory sequences associated with a genetic locus, said method comprising the steps of:
  - (a) providing a sample containing nuclear chromatin;
  - (b) treating said sample with an agent that induces modifications in DNA at hypersensitivity sites; and
  - (c) identifying the DNA hypersensitivity sites induced by the agent; thereby generating an regulatory sequence profile associated with the genetic locus.
2. The method of claim 1, wherein the regulatory sequence profile comprises nucleotide sequences of said DNA hypersensitivity sites and the locations thereof within the genetic locus.
3. The method of claim 1, wherein the genetic locus comprises the coding region for at least one expressed gene.
4. The method of claim 3, wherein the gene is a known gene.
5. The method of claim 3, wherein the gene is associated with a disease state.
6. The method of claim 5, wherein the disease state is a cancer.
7. The method of claim 5, wherein the gene is selected from the group consisting of: p53, Rb, INK4A/p16, CTNNB1, H-Ras, Fos, MDM2, INK4, ARF1, PTEN, Jun, WNT3A/14, NFkB, TERT, BRCA1, BRCA2, WAF1/p21, CDK4, TGF-beta1, RAR, E2F, VHL, MLH1, SMAD4, SMAD2, SMAD3, K-Ras, EGFR, WT1, Myc, Raf, ABL, and HER2.
8. The method of claim 1, wherein the genetic locus comprises greater than about 1 kb of DNA.

9. The method of claim 1, wherein the genetic locus comprises greater than about 10 kb of DNA.
10. The method of claim 1, wherein the genetic locus comprises greater than about 25 kb of DNA.
11. The method of claim 1, wherein the genetic locus comprises greater than about 50 kb of DNA.
12. The method of claim 1, wherein the genetic locus comprises greater than about 100 kb of DNA.
13. The method of claim 1, wherein the genetic locus comprises about 1 to 100 kb of DNA.
14. The method of claim 1, wherein the genetic locus comprises about 25 to 75 kb of DNA.
15. The method of claim 1, wherein the genetic locus comprises about 50 to 100 kb of DNA.
16. The method of claim 1, wherein the step of identifying regulatory sequences associated with said genetic locus is performed by a plurality of polymerase chain reactions.
17. The method of claim 16, wherein the polymerase chain reactions employ primers that amplify products spanning substantially the entirety of the genetic locus.
18. The method of claim 17, wherein said products comprise DNA sequences having lengths between about 100 and 1000 base pairs.

19. The method of claim 17, wherein said products comprise DNA sequences having lengths between about 100 and 500 base pairs.
20. The method of claim 17, wherein said products comprise DNA sequences having lengths between about 200 and 300 base pairs.
21. The method of claim 1, wherein said agent that induces modifications in DNA at hypersensitivity sites is selected from the group consisting of radiation, a chemical agent, an enzyme, and combinations thereof.
22. The method of claim 21, wherein the radiation comprises UV light radiation.
23. The method of claim 21, wherein the chemical agent is a clastogen.
24. The method of claim 21, wherein the enzyme is selected from the group consisting of specific endonucleases, non-specific endonucleases, topoisomerases, methylases, histone acetylases, histone deacetylases, and combinations thereof.
25. The method of claim 24, wherein the specific endonuclease comprises one or more four-base restriction endonucleases, one or more six-base restriction endonucleases, or combinations thereof.
26. The method of claim 25, wherein the four-base restriction endonuclease is selected from the group consisting of Sau3a, Styl, Nla III, Hsp 92, and combinations thereof.
27. The method of claim 25, wherein the six-base endonuclease is selected from the group consisting of EcoRI, HindIII, and combinations thereof.
28. The method of claim 24, wherein the non-specific endonuclease is DNase I.

29. The method of claim 24, wherein the topoisomerase is topoisomerase II.
30. The method of claim 1, wherein the genetic locus comprises DNA isolated from the group of organisms consisting of Homo sapien, rat, mouse, zebrafish, drosophila, yeast, C. elegans, and combinations thereof.
31. An isolated DNA hypersensitivity site identified according to the method of any one of claims 1-30.
32. An regulatory sequence profile identified according to the method of any one of claims 1-30.
33. A nucleotide array comprising a plurality of regulatory sequence sequences identified by the method of any one of claims 1-30.
34. The nucleotide array of claim 33, wherein the array is fixed to a slide, a chip, or a membrane filter.
35. The nucleotide array of claim 33, wherein one or more copies of said nucleotide sequences of the hypersensitive sites are spotted on said array.
36. A method of ascertaining the effect of an agent or other environmental perturbation on an regulatory sequence profile of a genetic locus comprising;
  - (a) obtaining a first regulatory sequence profile associated with the genetic locus, wherein the sample from which the regulatory sequences are identified is unexposed to the agent or perturbation;
  - (b) obtaining a second regulatory sequence profile associated with the genetic locus, wherein the sample from which the regulatory sequences are identified is exposed to the agent or perturbation; and
  - (c) comparing the first profile with the second profile to determine regulatory sequences that are effected by the agent perturbation.

37. The method of claim 36, wherein the perturbation occurs before obtaining the sample from a tissue, wherein the environmental perturbation is selected from the group consisting of an infection of the eukaryotic organism from a microorganism, loss in immune function of the eukaryotic organism, exposure of the tissue to high temperature, exposure of the tissue to low temperature, cancer of the tissue, cancer of another tissue in the eukaryotic organism, irradiation of the tissue, exposure of the tissue to a chemical or other pharmaceutical compound; and aging.
38. The method of claim 36, wherein the perturbation occurs after obtaining the sample from a tissue, wherein the perturbation is selected from the group consisting of exposure of the tissue to high temperature, exposure of the tissue to low temperature, irradiation of the tissue, exposure of the tissue to a chemical or other pharmaceutical compound, and aging.
39. The method of claim 36, wherein the perturbation is the addition of one or more compounds.
40. A method for profiling differential regulatory sequence activation associated with a genetic locus, comprising:
- (a) obtaining multiple regulatory sequences associated with the genetic locus from a first population and labeling them with a first label;
  - (b) obtaining multiple regulatory sequences associated with the genetic locus from a second population and labeling them with a second label;
  - (c) hybridizing the elements from a) and the fragments from b) with a DNA microarray containing DNA species in separate locations that match putative or verified regulatory elements associated with the genetic locus; and
  - (d) determining the ratio of signals from the first and second labels within the array.
41. The method of claim 40, wherein one of the populations is an untreated control and the other population is treated by contact with at least one agent,

and the signal ratios obtained in step d) provide an indication of gene regulatory activity modulated by the agent.

42. A method of identifying a gene associated with a disease or disorder, comprising:
  - (a) comparing an regulatory sequence profile of a cell with a disease or disorder to an regulatory sequence profile of a normal control cell;
  - (b) identifying an regulatory sequence with different activities in the two cells, and
  - (c) identifying a gene associated with the regulatory sequence identified in step (b).
43. The method of claim 42, wherein the active chromatin profiles are associated with a known gene.
44. The method of claim 42, wherein the active chromatin profiles are associated with a specific chromatin region.
45. The method of claim 42, wherein the disease or disorder is a cancer.
46. The method of claim 42, wherein the comparison is performed using an array of regulatory sequence sequences.
47. The method of claim 46, wherein the array includes regulatory sequence sequences associated with a plurality of genes.
48. A method of identifying an regulatory sequence of a gene, comprising:
  - (a) preparing an regulatory sequence profile of a gene; and
  - (b) identifying an regulatory sequence within the profile.
49. The method of claim 48, wherein the regulatory sequence profile is prepared according to the method of claim 1.

50. A method of identifying an allelic form of a gene, comprising:
- (a) comparing an regulatory sequence profile of one cell to an regulatory sequence profile of a second cell, wherein the regulatory sequence profiles are associated with the same gene; and
  - (b) identifying an regulatory sequence displaying different activities in the two cells.
51. The method of claim 50, further comprising obtaining the sequence of at least one of the identified regulatory sequences.
52. A method of identifying a cell, comprising:
- (a) determining the regulatory sequence profile associated with a cell;
  - (b) comparing the regulatory sequence profile of the cell to an regulatory sequence profile associated with a known cell types; and
  - (c) identifying a cell type with the same or a substantially similar regulatory sequence profile as the cell,
- thereby identifying the cell type of the cell.
53. The method of claim 52, wherein the comparison is performed using an array of polynucleotides comprising regulatory sequences.
54. A method of detecting a disease or disorder in a subject, comprising:
- (a) identifying an regulatory sequence profile associated with a disease or disorder;
  - (b) determining an regulatory sequence profile of a subject; and
  - (c) comparing the regulatory sequence profile of the subject to the regulatory sequence profile associated with the disease or disorder, wherein the same or a similar regulatory sequence profile indicates the presence of the disease or disorder, and wherein the regulatory sequence profiles are associated with the same genetic locus.

55. A method of qualifying a patient for a clinical trial, comprising:
- (a) identifying an regulatory sequence profile of a patient, and
  - (b) comparing the regulatory sequence profile of the patient to an regulatory sequence profile identified in patients suitable for a clinical trial, wherein the regulatory sequence profiles are associated with the same genetic locus.
56. A method of selecting a therapy for a patient, comprising:
- (a) identifying an regulatory sequence profile of a patient;
  - (b) comparing the regulatory sequence profile identified in step (a) to the regulatory sequence profile associated with a favorable outcome following a therapy; and
  - (c) selecting the therapy if the regulatory sequence profiles are the same or substantially similar.
57. A method of predicting the outcome of a disease or treatment protocol, comprising:
- (a) identifying an regulatory sequence profile of a patient;
  - (b) comparing the regulatory sequence profile identified in step (a) to the regulatory sequence profiles associated with one or more outcomes associated with a disease or treatment; and
  - (c) identifying an regulatory sequence profiles associated with an outcome associated with a disease or treatment that is the same or substantially similar to the regulatory sequence profile identified in step (a).
58. A method of screening a drug candidate, comprising:
- (a) identifying one or more regulatory sequence profiles associated with a cell with a disease or disorder, wherein the cell is not treated with a candidate drug;
  - (b) providing the candidate drug to a cell with the disease or disorder;
  - (c) identifying one or more regulatory sequence profiles associated with the cell provided with the candidate drug; and



- (d) comparing the regulatory sequence profiles of steps (a) and (c) and thereby determining whether treatment with the candidate drug altered an regulatory sequence profile.
59. A method of identifying a drug useful in treating a disease or disorder, comprising:
- (a) identifying an regulatory sequence profile associated with a disease or disorder;
  - (b) treating a cell with the disease or disorder with a candidate drug;
  - (c) identifying an regulatory sequence profile after treatment with the candidate drug, wherein the regulatory sequence profiles correspond to the same genetic locus; and
  - (d) comparing the regulatory sequence profiles of steps (a) and (c) to determine if treatment with the candidate drug affected the regulatory sequence profile.
60. A drug identified according to the method of claim 59.
61. A method of manufacturing a drug, comprising:
- (a) identifying a drug that alters an regulatory sequence profile associated with a disease or disorder; and
  - (b) manufacturing the identified drug.
62. A computer readable medium comprising an regulatory sequence profile associated with a genetic locus.
63. The computer readable medium of claim 62, wherein the genetic locus comprises an open reading frame.
64. The computer readable medium of claim 63, wherein the open reading frame encodes a gene associated with a disease or disorder.

65. The computer readable medium of claim 64, wherein the disease or disorder is a cancer.
66. The computer readable medium of claim 64, wherein the gene is selected from the group consisting of: p53, Rb, INK4A/p16, CTNNB1, H-Ras, Fos, MDM2, INK4, ARF1, PTEN, Jun, WNT3A/14, NFkB, TERT, BRCA1, BRCA2, WAF1/p21, CDK4, TGF-beta1, RAR, E2F, VHL, MLH1, SMAD4, SMAD2, SMAD3, K-Ras, EGFR, WT1, Myc, Raf, ABL, and HER2.
67. The computer readable medium of claim 66, wherein the active chromatin profile contains the genomic position and activity of one or more regulatory sequences.
68. The computer readable medium of claim 67, wherein the genetic locus comprises an open reading frame.
69. A computer readable medium comprising a plurality of regulatory sequence profiles associated with a specific cell.
70. The computer readable medium of claim 69, wherein the cell is a mammalian cell.
71. The computer readable medium of claim 69, wherein the cell is a diseased cell.
72. The computer readable medium of claim 69, wherein the regulatory sequence profiles include the genetic location and activities of at least one regulatory sequence.
73. A computer readable medium comprising a plurality of regulatory sequence profiles associated with different cells.

74. The computer readable medium of claim 73, wherein the regulatory sequence profiles are associated with the same genetic locus.
75. The computer readable medium of claim 73, wherein the regulatory sequence profiles include regulatory sequence profiles associated with a plurality of genetic loci for each cell.
76. The computer readable medium of claim 73, wherein one or more cells is treated with an agent.
77. The computer readable medium of claim 76, wherein the agent is a drug candidate.
78. The computer readable medium of claim 73, wherein the cells are derived from different tissues.
79. The computer readable medium of claim 73, wherein one or more cells is a diseased cell.
80. A computer readable medium comprising regulatory sequence profiles for at least two genetic loci, wherein each locus comprises an open reading frame and one or more regulatory sequences associated with that gene, and wherein the profile includes polynucleotide sequences selected from the group consisting of:
  - (a) sequences of open reading frames
  - (b) sequences that hybridize to a an open reading frame under moderately stringent conditions;
  - (c) degenerate sequences of open reading frames; and
  - (d) sequences that hybridize to degenerate sequences of open reading frames.
81. The computer readable medium of claim 80 comprising the sequences for at least one gene selected from the group consisting of: p53, Rb, INK4A/p16,

CTNNB1, H-Ras, Fos, MDM2, INK4, ARF1, PTEN, Jun, WNT3A/14, NFkB, TERT, BRCA1, BRCA2, WAF1/p21, CDK4, TGF-beta1, RAR, E2F, VHL, MLH1, SMAD4, SMAD2, SMAD3, K-Ras, EGFR, WT1, Myc, Raf, ABL, and HER2.

82. The computer readable medium of claim 80, wherein at least one regulatory sequence is a promoter or enhancer of transcription for a gene.
83. A computer executable program for comparing regulatory sequence profiles of two or more cells, comprising:
  - (a) inputting an regulatory sequence profile associated with a genetic locus in a first cell;
  - (b) inputting an regulatory sequence profile associated with the same genetic locus in a second cell; and
  - (c) outputting a comparison of the regulatory sequence profiles of steps (a) and (b).
84. A computer executable program for the identification of a cell, comprising:
  - (a) inputting an regulatory sequence profile associated with one or more genetic loci in a cell;
  - (b) searching a data set comprising regulatory sequence profiles for the same genetic loci in one or more known cell types; and
  - (c) outputting a cell type with the same or a substantially similar regulatory sequence profile as the regulatory sequence profile of step (a).
85. A method of regulating gene expression, comprising:
  - (a) identifying an regulatory sequence profile associated with a desired pattern of gene expression;
  - (b) preparing a nucleic acid vector comprising at least a plurality of regulatory sequences within the profile of step (a) operably linked to a gene sequence; and
  - (c) introducing the vector into a cell.

86. The method of claim 85, wherein the cell is stably introduced into the cell to obtain permanent heritable transmission of the regulatory sequences and operably linked gene sequence.
87. The method of claim 85, wherein the gene encodes a regulatory protein.
88. The method of claim 85, wherein the gene encodes a therapeutic molecule.
89. The method of claim 88, wherein the therapeutic molecule is a polypeptide or a polynucleotide.
90. The method of claim 89, wherein the therapeutic molecule is selected from the group consisting of: ribozymes, antisense RNA, double-stranded RNA, small interfering RNA, and short hairpin RNA.
91. A regulatory sequence identified by the method of claim 48.
92. An allelic variant identified by the method of claim 50.
93. A computer executable program for profiling a genetic locus for active chromatin, comprising inputting data comprising regions of chromatin hypersensitivity sites derived from a selected cell or tissue type; comparing said data with data derived from the different cell or tissue type or with a control data set; and outputting at least one sequence associated with said locus or a genomic location of said active chromatin.
94. The method of claim 93, wherein said inputted data comprises sequences of chromatin hypersensitive sites generated by enzymatic digestion of chromatin.

95. The method of claim 93, wherein said inputted data comprises sequences of chromatin hypersensitive sites generated by using thermostable polymerase amplification of preselected regions of the genome.
96. The method of claim 93, wherein said preselected regions are within 500 kb of a gene known to be associated with a disease state.
97. A computer executable program for profiling a genetic locus for allelic variants affecting the formation of active chromatin, comprising inputting data comprising regions of chromatin hypersensitivity sites derived from a selected mammalian cell or tissue type; comparing said data with data derived from the same cell or tissue type isolated from another mammal of the same species with a control data set representing normal or expected sequences from said species; and outputting at least one sequence having an allelic variant affecting said active chromatin formation.
98. A regulatory profile platform comprising regulatory sequences associated with a plurality of genetic loci in a plurality of different cell types.
99. A method for profiling chromatin sensitivity of a genomic region of cells of a cell type to digestion by a DNA modifying agent, comprising determining a chromatin sensitivity profile, said chromatin sensitivity profile comprising a plurality of replicate measurements of each of a plurality of different genomic sequences in said genomic region, wherein each of said plurality of replicate measurements is a ratio of (i) copy numbers of an amplicon comprising said genomic sequence measured by real-time quantitative PCR (qPCR) with chromatin of said cell type that has been treated with said DNA modifying agent and (ii) copy numbers of said amplicon measured by real-time qPCR with chromatin of said cell type that has not been treated with said DNA modifying agent.

100. The method of claim 99, wherein said plurality of different genomic sequences comprises successively overlapping sequences tiled across one or more portions of said genomic region.
101. The method of claim 100, wherein said plurality of different genomic sequences comprises successively overlapping sequences tiled across said genomic region.
102. The method of claim 99, wherein each of said plurality of different genomic sequences has a length in the range of about 75 to about 300 bases.
103. The method of claim 102, wherein the mean length of said plurality of different genomic sequences is about 250 bases.
104. The method of claim 99, wherein said plurality of duplicate measurements consists of at least 3 duplicate measurements.
105. The method of claim 104, wherein said plurality of duplicate measurements consists of at least 6 duplicate measurements.
106. The method of claim 105, wherein said plurality of duplicate measurements consists of at least 9 duplicate measurements.
107. The method of claim 99, further comprising determining a baseline chromatin sensitivity profile by a method comprising  
(a) smoothing the data in said chromatin sensitivity profile to obtain a baseline curve;  
and  
(b) determining the error bounds for said baseline curve,  
wherein said baseline curve and said error bounds constitute said baseline chromatin profile.
108. The method of claim 107, wherein said smoothing is carried out using LOWESS.

109. The method of claim 107, wherein said error bounds are determined by a method comprising

- (b1) mean centering said plurality of replicates for each genomic sequence in said chromatin sensitivity profile about said baseline curve to generate a mean-centered chromatin sensitivity profile, wherein said mean-centering is carried out by setting the mean of each said plurality of replicates to the value of the corresponding genomic sequence on said baseline curve;
- (b2) determining the median M of said mean-centered chromatin sensitivity profile;
- (b3) determining the Median Absolute Deviation MAD of said mean-centered chromatin sensitivity profile;
- (b4) discarding for each genomic sequence replicate measurement X if X satisfy equation

$$\frac{|X - M|}{MAD / 0.6745} > 2.24, \text{ and}$$

- (b5) defining the error bounds as the lower and upper confidence limits on the remaining data.

110. The method of claim 107, wherein said error bounds are determined by a method comprising

- (b1) generating a bootstrap chromatin sensitivity profile by randomly selecting one replicate measurement from said plurality of replicate measurements for each genomic sequence;
- (b2) mean centering said plurality of replicates for each genomic sequence in said bootstrap chromatin sensitivity profile about said baseline curve to generate a mean-centered chromatin sensitivity profile, wherein said mean-centering is carried out by setting the mean of each said plurality of replicates to the value of the corresponding genomic sequence on said baseline curve;
- (b3) determining the median M of said mean-centered chromatin sensitivity profile;
- (b4) determining the Median Absolute Deviation MAD of said mean-centered chromatin sensitivity profile;
- (b5) discarding for each genomic sequence replicate measurement X if X satisfy equation

$$\frac{|X - M|}{MAD / 0.6745} > 2.24,$$



- (b5) determining the maximum lower and minimum upper outliers on the remaining data;
- (b6) repeating said step (b1)-(b5) for a plurality of times; and
- (b7) calculating the upper and lower outlier cutoff values and Bca confidence intervals.

111. The method of claims 109, further comprising

- (c1) identifying one or more genomic sequences among said plurality of genomic sequences whose 20% trimmed means lie outside said error bounds; and
- (c2) determining a signal-to-noise ratio S/N of said identified genomic sequences according to equation

$$S/N_i = \frac{|HS_i - B_i|}{MAD_B(\sigma_c / \sigma_{HS})^2}$$

where  $S/N_i$  is the signal-to-noise ratio at site  $i$ ,  $HS_i$  is the Y% trimmed mean of the corresponding HS cluster,  $B_i$  is the value of said baseline curve at said site  $i$ ,  $MAD_B$  is the median average deviation of the centered baseline,  $\sigma_{HS}$  is the average variance of replicate measurements, and  $\sigma_c$  is the variance of the replicate measurements at said site  $i$ .

112. The method of claims 110, further comprising

- (c1) identifying one or more genomic sequences among said plurality of genomic sequences whose 20% trimmed means lie outside said error bounds; and
- (c2) determining a signal-to-noise ratio S/N of said identified genomic sequences according to equation

$$S/N_i = \frac{|HS_i - B_i|}{MAD_B(\sigma_c / \sigma_{HS})^2}$$

where  $S/N_i$  is the signal-to-noise ratio at site  $i$ ,  $HS_i$  is the Y% trimmed mean of the corresponding HS cluster,  $B_i$  is the value of said baseline curve at said site  $i$ ,  $MAD_B$  is the median average deviation of the centered baseline,  $\sigma_{HS}$  is the average variance of replicate measurements, and  $\sigma_c$  is the variance of the replicate measurements at said site  $i$ .

113. The method of any one of claims 99-112, wherein each said copy number has been corrected for amplification efficiency.
114. The method of any one of claims 99-112, wherein said DNA modifying agent is DNase I.
115. The method of any one of claims 99-112, wherein each of said plurality of duplicated measurements is measured by independent real-time qPCR experiments.
116. The method of any one of claims 99-112, wherein each of said plurality of duplicated measurements is measured by independent real-time qPCR experiments using different treated chromatin samples.
117. A method for profiling chromatin sensitivity of a genomic region of cells of a cell type to digestion by a DNA modifying agent, comprising
- (a) treating chromatin of cells of said cell type with said DNA modifying agent such that digestion of DNA occurs and retrieving DNA molecules;
  - (b) amplifying a plurality of different genomic sequences in said genomic region by real-time quantitative PCR using at least a portion of said retrieved DNA molecules and determining copy numbers of amplification product of each said genomic sequence;
  - (c) amplifying said plurality of different genomic sequences in said genomic region by real-time quantitative PCR using DNA molecules obtained from chromatin of cells of said cell type that is not treated by said DNA modifying agent and determining copy numbers of amplification product of each said genomic sequence;
  - (d) determining a ratio of said copy numbers measured in step (b) and copy numbers measured in said step (c)
  - (e) repeating said steps (b) - (d) a plurality of times to generate a plurality of ratios, thereby generating a plurality of replicate measurements for each of said genomic sequences; and
  - (d) determining a chromatin sensitivity profile of said genomic region, said chromatin sensitivity profile comprising said plurality of replicate measurements.

118. The method of claim 117, wherein said plurality of different genomic sequences comprises successively overlapping sequences tiled across one or more portions of said genomic region.
119. The method of claim 118, wherein said plurality of different genomic sequences comprises successively overlapping sequences tiled across said genomic region.
120. The method of claim 117, wherein each of said plurality of different genomic sequences has a length in the range of about 75 to about 300 bases.
121. The method of claim 120, wherein the mean length of said plurality of different genomic sequences is about 250 bases.
122. The method of claim 117, wherein said plurality of duplicate measurements consists of at least 3 duplicate measurements.
123. The method of claim 122, wherein said plurality of duplicate measurements consists of at least 6 duplicate measurements.
124. The method of claim 123, wherein said plurality of duplicate measurements consists of at least 9 duplicate measurements.
125. The method of claim 117, further comprising determining a baseline chromatin sensitivity profile by a method comprising  
(a) smoothing the data in said chromatin sensitivity profile to obtain a baseline curve;  
and  
(b) determining the error bounds for said baseline curve,  
wherein said baseline curve and said error bounds constitute said baseline chromatin profile.
126. The method of claim 125, wherein said smoothing is carried out using LOWESS.

127. The method of claim 125, wherein said error bounds are determined by a method comprising

(b1) mean centering said plurality of replicates for each genomic sequence in said chromatin sensitivity profile about said baseline curve to generate a mean-centered chromatin sensitivity profile, wherein said mean-centering is carried out by setting the mean of each said plurality of replicates to the value of the corresponding genomic sequence on said baseline curve;

(b2) determining the median M of said mean-centered chromatin sensitivity profile;

(b3) determining the Median Absolute Deviation MAD of said mean-centered chromatin sensitivity profile;

(b4) discarding for each genomic sequence replicate measurement X if X satisfy equation

$$\frac{|X - M|}{MAD/0.6745} > 2.24, \text{ and}$$

(b5) defining the error bounds as the lower and upper confidence limits on the remaining data.

128. The method of claim 125, wherein said error bounds are determined by a method comprising

(b1) generating a bootstrap chromatin sensitivity profile by randomly selecting one replicate measurement from said plurality of replicate measurements for each genomic sequence;

(b2) mean centering said plurality of replicates for each genomic sequence in said bootstrap chromatin sensitivity profile about said baseline curve to generate a mean-centered chromatin sensitivity profile, wherein said mean-centering is carried out by setting the mean of each said plurality of replicates to the value of the corresponding genomic sequence on said baseline curve;

(b3) determining the median M of said mean-centered chromatin sensitivity profile;

(b4) determining the Median Absolute Deviation MAD of said mean-centered chromatin sensitivity profile;

(b5) discarding for each genomic sequence replicate measurement X if X satisfy equation

$$\frac{|X - M|}{MAD/0.6745} > 2.24,$$

- (b5) determining the maximum lower and minimum upper outliers on the remaining data;
- (b6) repeating said step (b1)-(b5) for a plurality of times; and
- (b7) calculating the upper and lower outlier cutoff values and Bca confidence intervals.

129. The method of claims 127, further comprising

- (c1) identifying one or more genomic sequences among said plurality of genomic sequences whose 20% trimmed means lie outside said error bounds; and
- (c2) determining a signal-to-noise ratio S/N of said identified genomic sequences according to equation

$$S/N_i = \frac{|HS_i - B_i|}{MAD_B(\sigma_c / \sigma_{HS})^2}$$

where  $S/N_i$  is the signal-to-noise ratio at site  $i$ ,  $HS_i$  is the Y% trimmed mean of the corresponding HS cluster,  $B_i$  is the value of said baseline curve at said site  $i$ ,  $MAD_B$  is the median average deviation of the centered baseline,  $\sigma_{HS}$  is the average variance of replicate measurements, and  $\sigma_c$  is the variance of the replicate measurements at said site  $i$ .

130. The method of claims 127, further comprising

- (c1) identifying one or more genomic sequences among said plurality of genomic sequences whose 20% trimmed means lie outside said error bounds; and
- (c2) determining a signal-to-noise ratio S/N of said identified genomic sequences according to equation

$$S/N_i = \frac{|HS_i - B_i|}{MAD_B(\sigma_c / \sigma_{HS})^2}$$

where  $S/N_i$  is the signal-to-noise ratio at site  $i$ ,  $HS_i$  is the Y% trimmed mean of the corresponding HS cluster,  $B_i$  is the value of said baseline curve at said site  $i$ ,  $MAD_B$  is the median average deviation of the centered baseline,  $\sigma_{HS}$  is the average variance of replicate measurements, and  $\sigma_c$  is the variance of the replicate measurements at said site  $i$ .

131. The method of any one of claims 117-130, wherein each said copy number has been corrected for amplification efficiency.
132. The method of any one of claims 117-131, wherein said DNA modifying agent is DNase I.
133. The method of any one of claims 117-130, wherein each of said plurality of duplicated measurements is measured by independent real-time qPCR experiments.
134. The method of any one of claims 117-130, wherein each of said plurality of duplicated measurements is measured by independent real-time qPCR experiments using different treated chromatin samples.
135. The method of any one of claims 111-112 and 129-130, wherein said Y% trimmed mean is 20% trimmed mean.